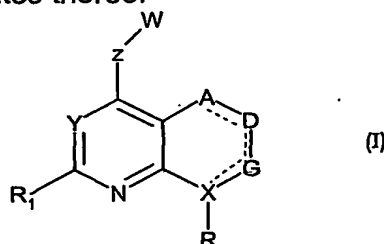


Claims

1. Compounds of formula (I) including stereoisomers, prodrugs and pharmaceutically acceptable salts or solvates thereof



wherein

the dashed line may represent a double bond;

R is aryl or heteroaryl, each of which may be substituted by 1 to 4 groups J selected from:

halogen, C1-C6 alkyl, C1-C6 alkoxy, halo C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, halo C1-C6 alkoxy, -C(O)R₂, nitro, hydroxy, -NR₃R₄, cyano, and or a group Z;

R₁ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 thioalkyl, C2-C6 alkenyl, C2-C6 alkynyl, halo C1-C6 alkyl, halo C1-C6 alkoxy, halogen, NR₃R₄ or cyano;

R₂ is a C1-C4 alkyl, -OR₃ or -NR₃R₄;

R₃ is hydrogen or C1-C6 alkyl;

R₄ is hydrogen or C1-C6 alkyl;

R₅ is a C1-C6 alkyl, halo C1-C6 alkyl, C1-C6 alkoxy, halo C1-C6 alkoxy, C3-C7 cycloalkyl, hydroxy, halogen, nitro, cyano, -NR₃R₄; -C(O)R₂;

R₆ is a C1-C6 alkyl, halo C1-C6 alkyl, C1-C6 alkoxy, halo C1-C6 alkoxy, C3-C7 cycloalkyl, hydroxy, halogen, nitro, cyano, -NR₃R₄; -C(O)R₂;

R₇ is hydrogen, C1-C6 alkyl, halogen or halo C1-C6 alkyl;

R₈ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR₃R₄ or cyano;

R₉ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR₃R₄ or cyano;

R₁₀ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR₃R₄ or cyano;

R₁₁ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR₃R₄ or cyano;

R₁₂ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR₃R₄ or cyano;

R₁₃ is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR₃R₄ or cyano;

R₁₄ is R₃ or -C(O)R₂;

D is CR₈R₉ or is CR₈ when double bonded with G or A;

- G is $CR_{10}R_{11}$ or is CR_{10} when double bonded with D or is CR_{10} when double bonded with X when X is carbon;
 A is $CR_{12}R_{13}$ or is CR_{12} when double bonded with D;
 X is carbon or nitrogen;
 Y is nitrogen or $-CR_7$;
 W is a 4-8 carbocyclic membered ring, which may be saturated or may contain one to three double bonds, and

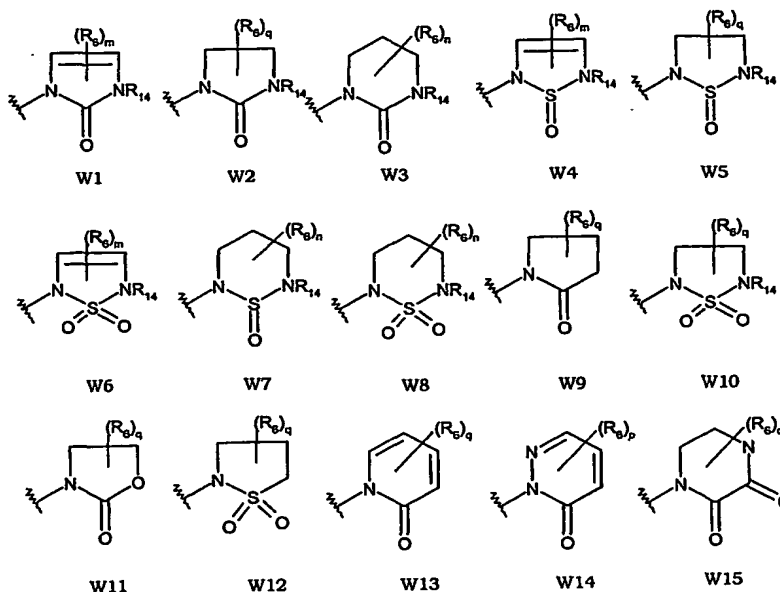
in which:

- one carbon atom is replaced by a carbon, I or $S(O)_m$; and
- one to four carbon atoms may optionally be replaced by oxygen, nitrogen or NR_{14} , $S(O)_m$, carbonyl, and such ring may be further substituted by 1 to 8 R_6 groups;

Z is a 5-6 membered heterocycle or a phenyl, which may be substituted by 1 to 8 R_5 groups;

m is an integer from 0 to 2.

2. Compounds according to claim 1, in which W is selected among the following groups:



in which:

W1 represents a 1,3-dihydro-2H-imidazol-2-one derivative;

W2 represents a imidazolidin-2-one derivative;

W3 represents a tetrahydropyrimidin-2(1H)-one derivative;

W4 represents a 2,5-dihydro-1,2,5-thiadiazole 1-oxide derivative;

W5 represents a 1,2,5-thiadiazolidine 1-oxide derivative;

W6 represents a 2,5-dihydro-1,2,5-thiadiazole 1,1-dioxide derivative;

W7 represents a 1,2,6-thiadiazinane 1-oxide derivative;

W8 represents a 1,2,6-thiadiazinane 1,1-dioxide derivative;

W9 represents a pyrrolidin-2-one derivative;

W10 represents a 2,5-dihydro-1,2,5-thiadiazolidine 1,1-dioxide derivative;

W11 represents a 1,3-oxazolidin-2-one derivative;

W12 represents a isothiazolidine 1,1-dioxide derivative;

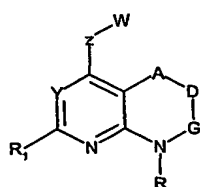
W13 represents a 2(1H)-pyridinone derivative;

W14 represents a 3(2H)-pyridazinone;

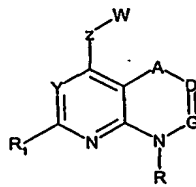
W15 represents a 2,3-piperazinedione derivative;

and q is an integer from 0 to 4, n is an integer from 0 to 6, p is an integer from 0 to 3 and m, R₆ and R₁₄ are defined as in claim 1.

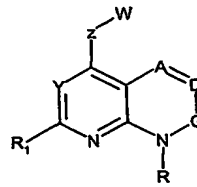
3. Compounds according to claims 1 and 2 of formula (la), (lb), (lc), (ld), and (le),



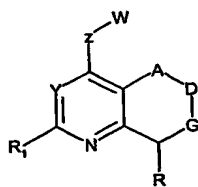
(la)



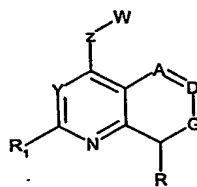
(lb)



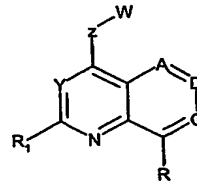
(lc)



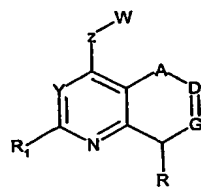
(ld)



(le)



(lf)



(lg)

in which R, R₁, Z, Y, W, A, D, G are defined as in claim 1 and 2.

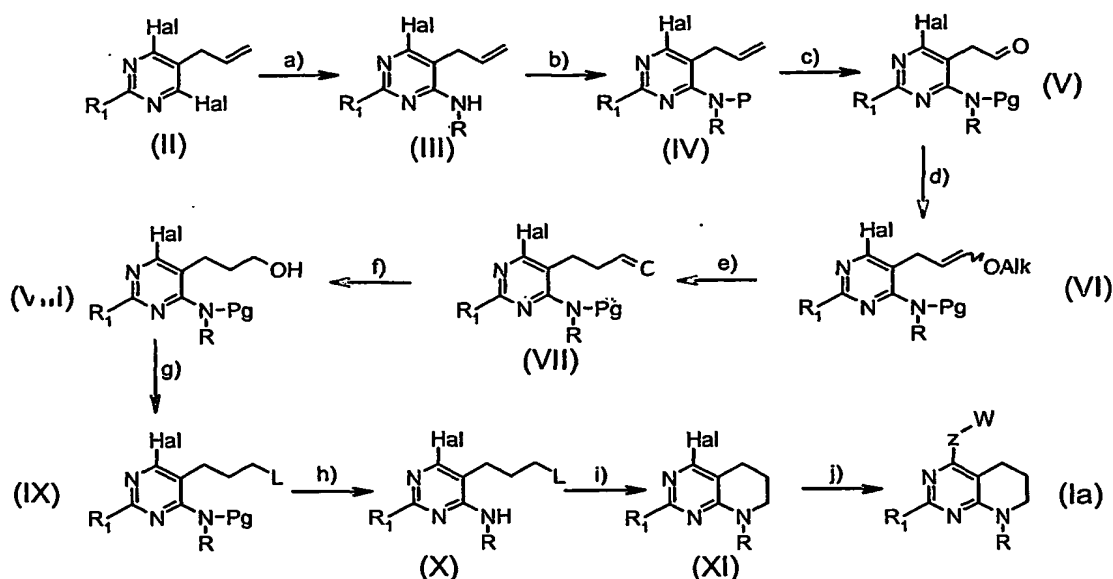
4. Compounds according to anyone of claims from 1 to 3, selected from the following group:

1-{1-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-4-yl]-1H-pyrazol-3-yl}-2-imidazolidinone;

1-{1-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydro-4-quinazolinyl]-1H-pyrazol-3-yl}-2-imidazolidinone;

1-{1-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydro-1,8-naphthyridin-4-yl]-1H-pyrazol-3-yl}-2-imidazolidinone.

5. Process for preparing compounds of formula (la) comprising the following steps:



in which

step a stands for the nucleophilic substitution with a suitable amine (such as a substituted aniline) of compounds of formula (II), in basic conditions (such as sodium hydride in a polar aprotic solvent) to give compounds (III);

step b stands for the protection of the amino group with a suitable protecting group (such as a BOC group);

step c stands for the oxidation of the double bond with a suitable oxidizing agent (such as ozone in a polar protic solvent) to give the aldehyde of compounds (V);

step d + e stands for formation of the aldehyde group of compounds (VII) through formation of the enol ether by Wittig reaction in the usual conditions, followed by acid hydrolysis (step e);

step f stands for the reduction of the aldehyde group of compounds (VII) to the alcohol of compounds (VIII) with a suitable reducing agent (such as sodium borohydride);

step g stands for the conversion of the alcohol of compounds (VIII) into a suitable leaving group (such as, for example, a halogen or reactive residue of sulphonic acid (e.g. mesylate, tosylate), preferably mesylate);

step h stands for the deprotection of the amino group of compounds (IX);

step i stands for the intramolecular cyclization to give the cyclized compounds (X)

step j stands for conversion of the halogen derivative, preferably chloride, into compounds (Ia), by reaction with the suitable reactive -Z-W derivative, in basic conditions (such as, for example, sodium hydride in a polar solvent).

6. The use of a compound according to anyone from claim 1 to 4, in the preparation of a medicament for use in the treatment of conditions mediated by CRF (corticotropin-releasing factor).
- 5 7. The use of a compound according to claim 6, in the preparation of a medicament for use in the treatment of depression and anxiety.
8. The use of a compound according claim 6, in the preparation of a medicament for use in the treatment of IBS (irritable bowel disease) and IBD (inflammatory bowel disease).
- 10
9. A compound according to anyone from claim 1 to 4, for use in the treatment of conditions mediated by CRF (corticotropin-releasing factor).
- 15 10. A pharmaceutical composition comprising a compound of anyone from claim 1 to 4, in admixture with one or more physiologically acceptable carriers or excipients.
11. A method for the treatment of a mammal, including man, in particular in the treatment of conditions mediated by CRF (corticotropin-releasing factor), comprising administration of an effective amount of a compound according to any of claims from 1 to 4.
- 20
12. A method, according to claim 11, in the treatment of depression and anxiety, comprising administration of an effective amount of a compound according to any of claims 1 to 4.
- 25
13. A method, according to claim 11, in the treatment of IBS (irritable bowel disease) and IBD (inflammatory bowel disease), comprising administration of an effective amount of a compound according to any of claims 1 to 4.
- 30